

-continued

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cc	1142

What is claimed is:

1. A non-human transgenic mammal whose genome comprises a modified SEQ ID NO: 2 encoding wild-type merozoite surface protein (MSP-1) operably linked to a mammary gland promoter,

wherein the modification reduces the AT content of SEQ

ID NO: 2 by 50% or less by replacement of protozoan codons with codons preferred by mammalian cells, wherein the replacement codons encode the same amino acid as the replaced codon, and

wherein the transgenic mammal expresses said modified SEQ ID NO: 2, thereby to produce MSP-1 in its milk.

2. The mammal of claim 1, wherein the promoter is a β -casein promoter.

3. The mammal of claim 1, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks at least one glycosylation site.

4. The mammal of claim 3, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks all glycosylation sites.

5. The mammal of claim 1, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 182.

6. The mammal of claim 1, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 263.

7. The mammal of claim 1, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising amino acid substitutions at positions 181 and 263. 182

8. A method of producing a merozoite surface protein 1 (MSP-1) in the milk of a non-human transgenic mammal, comprising:

35 providing a non-human transgenic mammal whose genome comprises a modified SEQ ID NO: 2 encoding wild-type MSP-1 operably linked to a mammary gland promoter, wherein the modification reduces the AT content of SEQ ID NO: 2 by 50% or less by replacement of protozoan codons with codons preferred by mammalian cells, wherein the replacement codons encode the same amino acid as the replaced codon; and

40 allowing the transgenic mammal to express said modified SEQ ID NO: 2, thereby to produce MSP-1 in its milk.

45 9. The method of claim 8, wherein the promoter is a β -casein promoter.

10. The method of claim 8, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks at least one glycosylation site.

50 11. The method of claim 10, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks all glycosylation sites.

55 12. The method of claim 8, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 182.

13. The method of claim 8, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 263.

60 14. The method of claim 8, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising amino acid substitutions at positions 181 and 263. 182

65 15. A non-human transgenic mammal whose genome comprises a modified SEQ ID NO: 2 encoding a wild-type MSP-1 operably linked to a mammary gland promoter,

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wherein the modification eliminates all the mRNA instability motifs in said SEQ ID NO: 2 by replacement of protozoan codons with codons preferred by mammalian cells,

wherein the replacement codons encode the same amino acid as the replaced codon, and

wherein the transgenic mammal expresses said modified SEQ ID NO: 2, to thereby produce MSP-1 in its milk.

16. The mammal of claim 15, wherein the promoter is a β -casein promoter.

17. The mammal of claim 15, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks at least one glycosylation site.

18. The mammal of claim 17, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks all glycosylation sites.

19. The mammal of claim 15, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 182.

20. The mammal of claim 15, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 263.

21. The mammal of claim 15, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising amino acid substitutions at positions 182 and 263.

22. A method of producing a merozoite surface protein 1 (MSP-1) sequence in the milk of a non-human transgenic mammal, comprising:

providing a non-human transgenic mammal whose genome comprises a modified SEQ ID NO: 2 encoding a wild-type MSP-1 operably linked to a mammary gland promoter,

wherein the modification eliminates all the mRNA instability motifs in said SEQ ID NO: 2 by replacement of protozoan codons with codons preferred by mammalian cells, and

wherein the replacement codons encode the same amino acid as the replaced codon; and,

allowing the transgenic mammal to express said modified SEQ ID NO: 2, to thereby produce MSP-1 in its milk.

23. The method of claim 22, wherein the promoter is a β -casein promoter.

24. The method of claim 22, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks at least one glycosylation site.

25. The method of claim 24, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks all glycosylation sites.

26. The method of claim 22, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 182.

27. The method of claim 22, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 263.

28. A transgenic non-human mammal whose genome comprises a modified SEQ ID NO: 2 encoding a wild-type MSP-1 operably linked to a mammary gland specific promoter, wherein the modification eliminates all the mRNA instability motifs of said SEQ ID NO: 2 by replacement of one or more protozoan codons with codons preferred by mammalian cells and the modification reduces the AT content of said SEQ ID NO: 2 by 50% or less by replacement of protozoan codons with codons preferred by mammalian cells, wherein the replacement codons encode the same amino acid as the replaced codon and wherein the transgenic mammal expresses said modified SEQ ID NO: 2, thereby to produce MSP-1 in its milk.

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29. The mammal of claim 28, wherein the modified SEQ ID NO: 2 is expressed in milk at a level which is at least 25% more than the wild-type sequence is expressed under the same conditions.

30. The mammal of claim 28, wherein the modified SEQ ID NO: 2 is expressed in milk at a level which is at least 50% more than the wild-type nucleic acid sequence is expressed under the same conditions.

31. The mammal of claim 28, wherein the modified SEQ ID NO: 2 is expressed in milk at a level which is at least 100% more than the wild-type nucleic acid sequence is expressed under the same conditions.

32. The mammal of claim 28, wherein all protozoan codons are replaced with codons preferred by mammalian cells.

33. The mammal of claim 28, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 182.

34. The mammal of claim 28, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 263.

35. The mammal of claim 28, wherein the promoter is a β -casein promoter.

36. A method for producing a merozoite surface protein 1 (MSP-1) sequence in the milk of a non-human transgenic mammal, comprising:

providing a non-human transgenic mammal whose genome comprises a modified SEQ ID NO: 2 encoding a wild-type MSP-1 operably linked to a mammary gland promoter, wherein the nucleic acid has been modified by a) elimination of mRNA instability motifs by the replacement of protozoan codons in SEQ ID NO: 2 with codons preferred by mammalian cells; and b) reduction of AT content by 50% or less by the replacement of one or more AT-containing protozoan codons of SEQ ID NO: 2 with codons preferred by mammalian cells,

wherein the replacement codons encode the same amino acid as the replaced codon; and

allowing the transgenic mammal to express said modified SEQ ID NO: 2, to thereby produce MSP-1 in its milk.

37. The method of claim 36, wherein the modified SEQ ID NO: 2 is expressed in milk at a level which is at least 25% more than the wild-type sequence is expressed under the same conditions.

38. The method of claim 36, wherein the modified SEQ ID NO: 2 is expressed in milk at a level which is at least 50% more than the wild-type nucleic acid sequence is expressed under the same conditions.

39. The method of claim 36, wherein the modified SEQ ID NO: 2 is expressed in milk at a level which is at least 100% more than the wild-type nucleic acid sequence is expressed under the same conditions.

40. The method of claim 36, wherein all protozoan codons are replaced with codons preferred by mammalian cells.

41. The method of claim 36, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 182.

42. The method of claim 36, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 263.

43. The method of claim 36, wherein the promoter is a beta casein promoter.